

**ABSTRACT**

The present invention relates to a method of inhibiting graft-versus-host  
5 disease in allogeneic hematopoietic stem cell transplant (HSCT) patients by using  
L-leucyl-L-leucine methyl ester (LLME) to eliminate selective cytotoxic T cells in  
donor lymphocyte infusions (DLI). LLME has been shown to inhibit GVHD in  
animal models by selectively inducing apoptosis in natural killer cells and cytotoxic T  
cells. The application of LLME to the human clinical HSCT situation, however, has  
10 been hampered by HSC toxicity when unseparated marrow is treated at the  
concentrations necessary to purge GVHD-inducing T cells prior to infusion. In the  
present invention, this problem is circumvented by the LLME *ex vivo* treatment of  
DLI administered following transplantation of T cell-depleted HSC. In this setting,  
the effects of LLME on HSC contained within the DLI are irrelevant for clinical  
15 outcome. In another embodiment, the risk of toxicity to the stem cell population is  
avoided by *ex vivo* LLME treatment of donor lymphocytes after separation of CD34<sup>+</sup>  
stem cells and then co-administration of the LLME-treated donor CD34<sup>+</sup> fraction and  
the untreated CD34<sup>+</sup> stem cells.